Complete Summary

GUIDELINE TITLE

Practice parameters for the dopaminergic treatment of restless legs syndrome and periodic limb movement disorder.

BIBLIOGRAPHIC SOURCE(S)

Littner MR, Kushida C, Anderson WM, Bailey D, Berry RB, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T, Li KK, Loube DL, Morgenthaler T, Wise M. Practice parameters for the dopaminergic treatment of restless legs syndrome and periodic limb movement disorder. Sleep 2004 May 1;27(3):557-9. [4 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- March 29, 2007, Permax (pergolide): Voluntary market withdrawal in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the U.S. Food and Drug Administration (FDA) Web site for more information.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Restless legs syndrome (RLS) and periodic limb movement disorder (PLMD)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Sleep Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To serve as a guide for the appropriate use of dopaminergic agents in the treatment of restless legs syndrome (RLS) and periodic limb movement disorder (PLMD)

TARGET POPULATION

Patients with restless legs syndrome (RLS) and periodic limb movement disorder (PLMD)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Levodopa with decarboxylase inhibitor
2. Pergolide*
3. Pramipexole
4. Ropinirole
5. Other dopamine agonists including talipexole cabergoline, piribedil, and alpha-dihydroergocryptine
6. Amantadine and selegiline

***Note from the National Guideline Clearinghouse (NGC)**: On March 29, 2007, Permax (pergolide) was withdrawn from the market in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the U.S. Food and Drug Administration (FDA) Web site for more information.

MAJOR OUTCOMES CONSIDERED

- Therapeutic efficacy of dopaminergic agents for treatment of RLS and PLMD
- Sleep parameters (total sleep time, sleep efficiency)
- Restless legs syndrome (RLS) and periodic leg movement disorder (PLMD) symptoms
- Adverse effects
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature searches were first conducted in January 2001, and then updated in August 2001 and finally, April 2002. The search was performed through Medline using the search terms: restless legs, periodic leg movement, periodic limb movement, and nocturnal myoclonus. A PubMed search was also done. Search terms were applied both to the keyword field and as a text search. A total of 227 papers were derived from the searches and reviewed for relevance to the therapeutic literature based on their abstracts. 56 papers were selected for detailed consideration and four were added by task force member recommendation from other search resources. Of these, 27 met the criteria of having a focus on restless legs syndrome (RLS) treatment with a minimum of 5 patients studied, a clear indication of restless legs syndrome or periodic limb movement disorder (PLMD) diagnosis for study entry, and use of a pharmaceutical agent which was primarily active on the dopamine system.

NUMBER OF SOURCE DOCUMENTS

27 articles were identified

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Level I (Grade A Recommendation): Large, well-designed, randomized and blinded controlled study with statistically significant conclusions on relevant variables

Level II (Grade B Recommendation): Smaller, well-designed, randomized and blinded controlled study with statistically significant conclusions on relevant variables

Level III (Grade C Recommendation): Well-designed, non-randomized prospective study with control group

Level IV (Grade C Recommendation): Well-designed, large prospective study with historical controls or careful attention to confounding effects or small prospective study with control group

Level V (Grade C Recommendation): Small prospective study or case series without control groups

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In most cases, the conclusions are based on evidence from studies published in peer-reviewed journals that were evaluated as noted in the evidence tables of the companion review paper in the original guideline document. When scientific data are absent, insufficient, or inconclusive, the recommendations are based upon consensus opinion.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Standard: This is a generally accepted patient-care strategy, which reflects a high degree of clinical certainty. The term standard generally implies the use of Level I Evidence, which directly addresses the clinical issue, or overwhelming Level II Evidence.

Guideline: This is a patient-care strategy, which reflects a moderate degree of clinical certainty. The term guideline implies the use of Level II Evidence or a consensus of Level III Evidence.

Option: This is a patient-care strategy, which reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

These recommendations were developed by the Standards of Practice Committee and reviewed and approved by the Board of Directors of the American Academy of Sleep Medicine.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Levels of recommendation (Standard, Guideline, and Option) and levels of evidence (I-V) are defined at the end of the "Major Recommendations" field.

1. Levodopa with decarboxylase inhibitor is effective in the treatment of restless legs syndrome (RLS) and periodic limb movement disorder (PLMD). (Hening et al., 2004; 4.b; Table 3) (**Standard**)
2. The dopamine agonist pergolide* is effective in the treatment of RLS and PLMD. (Hening et al., 2004; 4.c.ii; Table 4) (**Standard**)
3. The dopamine agonist pramipexole is effective in the treatment of RLS and PLMD. (Hening et al., 2004; 4.c.iii; Table 4) (**Guideline**)
4. The dopamine agonist ropinirole is effective in the treatment of RLS and PLMD. (Hening et al., 2004; 4.c.iv; Table 4) (**Option**)
5. Other dopamine agonists (talipexole, cabergoline, piribedil, and alpha-dihydroergocryptine) may be effective in the treatment of RLS or PLMD, but the level of effectiveness of these agonists is not currently established. (Hening et al., 2004; 4.c.v; Table 4) (**Option**)
6. The dopaminergic agents amantadine and selegiline may be effective in the treatment of RLS and PLMD, but the level of effectiveness of these agents is not currently established. (Hening et al., 2004; 4.d; Table 5) (**Option**)
7. No specific recommendations can be made regarding dopaminergic treatment of children or pregnant women with RLS or PLMD. (Hening et al., 2004; 5.b)

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Definitions:

Levels of Recommendation

Standard: This is a generally accepted patient-care strategy, which reflects a high degree of clinical certainty. The term standard generally implies the use of Level I Evidence, which directly addresses the clinical issue, or overwhelming Level II Evidence.

Guideline: This is a patient-care strategy, which reflects a moderate degree of clinical certainty. The term guideline implies the use of Level II Evidence or a consensus of Level III Evidence.

Option: This is a patient-care strategy, which reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.

Levels of Evidence

Level I (Grade A Recommendation): Large, well-designed, randomized, and blinded controlled study with statistically significant conclusions on relevant variables

Level II (Grade B Recommendation): Smaller, well-designed, randomized, and blinded controlled study with statistically significant conclusions on relevant variables

Level III (Grade C Recommendation): Well-designed, non-randomized prospective study with control group

Level IV (Grade C Recommendation): Well-designed, large prospective study with historical controls or careful attention to confounding effects or small prospective study with control group

Level V (Grade C Recommendation): Small prospective study or case series without control groups

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is specifically stated for each recommendation (See "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of dopaminergic agents in the treatment of restless legs syndrome (RLS) and periodic limb movement disorder (PLMD)

- Relief of RLS and PLMD symptoms
- Reduction of PLMS and PLMS-Waking Index
- Improvement in sleep parameters

POTENTIAL HARMS

Levodopa with Decarboxylase Inhibitor

The main side effects complicating the use of this agent in clinical series are the high frequencies of restless legs syndrome (RLS) daytime augmentation (i.e., occurrence or worsening of daytime RLS symptoms with long-term medication usage, typically increased by higher doses) and early morning rebound of RLS symptoms, especially at higher dose levels.

Pergolide

Adverse effects include nausea, congestion, and mild augmentation. In most cases, these adverse effects were either minor or could be adequately controlled; however, the development of pleuropulmonary fibrosis or cardiac valvulopathy has been reported in isolated case reports.

Pramipexole

The most common reported side effects in these studies were fluid retention/edema, daytime fatigue/sleepiness, gastrointestinal distress, insomnia/alertness, dizziness, and occasional augmentation of RLS.

Amantadine

In one study, side effects of drowsiness and fatigue were reported.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These practice parameters define principles of practice that should meet the needs of most patients in most situations. These guidelines should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed toward obtaining the same results. The ultimate judgment regarding the propriety of any specific care must be made by the physician in light of the individual circumstances presented by the patient and the available diagnostic and treatment options.
- These practice parameters reflect the state of knowledge at the time of development and will be reviewed, updated, and revised, as new information becomes available.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Littner MR, Kushida C, Anderson WM, Bailey D, Berry RB, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T, Li KK, Loube DL, Morgenthaler T, Wise M. Practice parameters for the dopaminergic treatment of restless legs syndrome and periodic limb movement disorder. Sleep 2004 May 1;27(3):557-9. [4 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 May 1

GUIDELINE DEVELOPER(S)

American Academy of Sleep Medicine - Professional Association

SOURCE(S) OF FUNDING

American Academy of Sleep Medicine

GUIDELINE COMMITTEE

Standards of Practice Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All authors of the accompanying review paper, members of the Standards of Practice Committee, and the American Academy of Sleep Medicine (AASM) Board of Directors completed detailed conflict-of-interest statements and were found to have none with regard to this subject.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Academy of Sleep Medicine (AASM) Web site.

Print copies: Available from the Standards of Practice Committee, American Academy of Sleep Medicine, One Westbrook Corporate Center, Suite 920, Westchester, IL 60154. Web site: www.aasmnet.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Hening WA, Allen RP, Earley CJ, Picchietti DL, Silber MH; Restless Legs Syndrome Task Force of the Standards of Practice Committee of the American Academy of Sleep Medicine. An update on the dopaminergic treatment of restless legs syndrome and periodic limb movement disorder. Sleep 2004 May;27(3):560-83.

Electronic copies: Available in Portable Document Format (PDF) from the American Academy of Sleep Medicine Web site.

Print copies: Available from the Standards of Practice Committee, American Academy of Sleep Medicine, One Westbrook Corporate Center, Suite 920, Westchester, IL 60154. Web site: www.aasmnet.org.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 2, 2005. The information was verified by the guideline developer on June 2, 2005. This summary was updated by ECRI Institute on May 8, 2007 following the U.S. Food and Drug Administration market withdrawal of Permax (pergolide).

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DISCLAIMER

NGC DISCLAIMER

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